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DETAILED ACTION

Status of Application, Amendments and/or Claims

The amendment of 08 January 2008 has been entered in full. Claims 1-25, 27, 30, 33-35, 38, 41-42, 44, 50, 57-58, 65-68, 70, and 72-153 have been cancelled and claims 26, 28-29, 31-32, 36-37, 39-40, 46, 53, 56, 59, 63-64, 71 have been amended. Claims 26, 28-29, 31-32, 36-37, 39-40, 43, 45 and 154-174 have been added.

Claims 26, 28-29, 31-32, 36-37, 39-40, 43, 45, 46, 49-50, 59-64, 68-69, 71, and 154-174 are pending and under examination.

Claim Objections

Applicant's amendments made to claim 60 and cancellation of claim 50 filed on 01/08/2008 have overcome the objection claims 49, 50, and 60. The objection of claims 49, 50, and 60 has been withdrawn.

New Claim Objections

Claim 28, 32, 46, and 47 are objected to because of the following informalities:

Claim 28 is dependent on claim 27, which has been cancelled.

Claim 32 is objected to because the Examiner cannot determine if the core recited in claim 32 refers to the magnetic core of claim 31, a different core, or an undefined core.

Applicants may obviate the rejection by amending claim 32 with "wherein the particles have a silica shell enveloping the core."

Claim 46 is objected to because claim 46 recites "0.1 HZ to 10 Hz". "0.1 HZ" should be replaced with "0.1 Hz".

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Claim 47 is objected to because it isn't clear as to what cells are being destroyed.

Applicants may obviate the rejection by amending the claim 47 with "destroying SAID cells."

Appropriate correction is required.

Rejections maintained

Claim Rejections - 35 USC § 112 (Written Description)

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 46, 49-50, 59-64, 68-69, and 71 remain rejected and the previously non-elected claims 26, 28-29, 31-32, 36-37, 39-40, 43, 45 and the newly added claims 154-174 are also rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 46, 49-50, 59-64, 68-69, and 71 and the previously non-elected claims 26, 28-29, 31-32, 36-37, 39-40, 43, 45 and the newly added 154-174 are also rejected, under 35 USC 112, first paragraph, for the reasons already of record on pages 4-6 of the Office Action mailed 07/12/2007.

At page 13 of the response, Applicants argue that the specification clearly describes the use of magnetisable particles to treat a disorder and in the regeneration of a tissue, such as cartilage, by associating a magnetisable particle with an ion channel of a cell. Specifically, Example 4 describes studies demonstrating the ability of a magnetic field to alter calcium

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channel activity following attachment of antibody-labeled magnetic particles to cells transfected with a Trek-1 construct.

Applicant's claim amendments have been fully considered but are not found persuasive. While Applicants have described a method of altering calcium channels in cells transfected with a TREK construct in the presence of an anti-TREK antibody bound to magnetic nanoparticles, Applicants have not provided sufficient disclosure regarding (A) a method of treating a patient suffering from a disorder involving an ion channel, and (B) a method of regenerating tissue, (C) a method of regenerating cartilage to be in possession of the claimed methods. For instance, Applicants have not provided any information regarding the molecules and cells involved in the claimed treatment methods.

In addition, Applicants have not satisfied the written description requirement because Applicants have not provided the correlation between the structural and functional characteristics for the disorder, the ion channel, magnetizable particles, and therapeutically agent utilized in the claimed method of treatment. While Applicants contend that the specification clearly describes the use of magnetisable particles to treat a disorder and the regeneration of a tissue and that Example 4 illustrates the use of the treatment method, Applicants have not provided any identifying characteristics for the disorder, the ion channel, magnetizable particles, and therapeutic agent recited in the claims. Thus Applicants are not in possession of the claimed invention because Applicants have not provided adequate description for the claimed methods as well as for the disorder, the ion channel, magnetizable particles, and therapeutic agent recited in the claims.

The addition of the previously non-elected claims 26, 28-29, 31-32, 36-37, 39-40, 43, 45, and addition of the newly added claims 154-174 have raised a new ground of rejection under 35 U.S.C. 112, first paragraph (Written Description).

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Claim 26 is drawn to a compound of elemental iron, a chromium compound, or a combination of any elemental iron or chromium compound. Claim 31 is drawn to a magnetic core with a biocompatible coating. Claim 39 is drawn to magnetizable particles with specific antibodies or protein binding motifs recognizing a cellular element with the cell. Claim 40 is drawn to cellular elements that include a transmembrane extracellular matrix molecule, a transmembrane adhesion molecule, a dispersed membrane adhesion protein, or an extracellular matrix. Claim 43 is drawn to a transmembrane adhesion molecule that includes integrin, cadherin, selectin, or immunoglobulin. Claim 156 is drawn to a magnetizable particle associated with an antibody. Claims 157, 163, 170 are drawn to an antibody that binds to a cellular element that includes a transmembrane extracellular matrix molecule, a transmembrane adhesion molecule, a dispersed membrane adhesion protein, or an extracellular matrix. Although the specification provides general description for compound of elemental iron, a chromium compound a magnetic core with a biocompatible coating, antibodies, protein binding motifs, a transmembrane extracellular matrix molecule, a transmembrane adhesion molecule, a dispersed membrane adhesion protein, an extracellular matrix, an integrin, a cadherin, a selectin, and an immunoglobulin recited in the claimed methods, the specification has not provided sufficient identifying structural and functions characteristics for anyone of them to satisfy the written description requirements.

Thus, the claims are genus claims. The specification and claims do not indicate what distinguishing attributes are shared by the members of the genera. Specifically, the specification does not clearly define a magnetic core with a biocompatible coating, antibodies, protein binding motifs, a transmembrane extracellular matrix molecule, an immunoglobulin and all methods of using such. Thus, the scope of the claims includes numerous structural and functional variants, and the genus is highly variant because a significant number of structural and functional

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differences between genus members is permitted. The specification and claims do not provide any guidance as to what changes should be made. Structural and functional features that could distinguish a magnetic core with a biocompatible coating, antibodies, protein binding motifs, a transmembrane extracellular matrix molecule and an immunoglobulin are missing from the disclosure. No common attributes identify the members of the genus. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, a magnetic core with a biocompatible coating, antibodies, protein binding motifs, a transmembrane extracellular matrix molecule, and an immunoglobulin are insufficient to describe the genus.

The written description requirement for a claimed genus' may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between structure and function structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genera. In the instant case, the specification fails to provide sufficient descriptive information, such as definitive structural or functional features of the genera for a magnetic core with a biocompatible coating, antibodies, protein binding motifs, a transmembrane extracellular matrix molecule, and an immunoglobulin and all methods of using such.

There is no description of the special features, which are critical to the structure and function of the genera claimed. Furthermore, the prior art does not provide compensatory structural or correlative teachings sufficient to enable one of skill to isolate and a magnetic core

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with a biocompatible coating, antibodies, protein binding motifs, a transmembrane extracellular matrix molecule, an immunoglobulin encompassed by the claims. Thus, no identifying characteristics or properties of a magnetic core with a biocompatible coating, antibodies, protein binding motifs, and an immunoglobulin are provided such that one of skill would be able to predictably identify the encompassed variant biological and chemical entities recited in the methods of the instant claims. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genera. Thus, applicant was not in possession of the claimed genus.

Claim Rejections - 35 USC § 112 (Enablement)

Claims 46, 49-50, 59-64, 68-69, and 71 remain rejected and the previously non-elected claims claims 26, 28-29, 31-32, 36-37, 39-40, 43, 45 and the newly added claims 154-174 are also rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for (A) up-regulation of osteopontin in response to a magnetic field in the presence of anti-TREK antibody bound to magnetic nanoparticles binding to TREK channel in mesenchymal cells, and (B) the production of cartilage in mice by implanted human mesenchymal stem cells in the presence of magnetic nanoparticles bound to cells via an anti-TREK antibody in response to time varying magnetic fields, does not reasonably provide enablement for (A) a method of treating a patient suffering from a disorder involving an ion channel, (B) a method of regenerating tissue, (C) a method of regenerating cartilage, (D) a method of treating a patient by destroying cells, inhibiting cell growth, or inducing osmotic shock to a cell, (E) a method of destroying tumor cells, (F) a method of killing cells by opening and closing ion channels, (G) a method of using ion channels to repair tissue and bone, and (H) a method comprising the generation of artificial tissue. The specification does not enable any person skilled in the art to

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which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Claims 46, 49-50, 59-64, 68-69, and 71 remain rejected and the previously non-elected claims 26, 28-29, 31-32, 36-37, 39-40, 43, 45 and the newly added claims 154-174 are also rejected, under 35 USC 112, first paragraph, in view of the amendments and declaration filed 01/08/2008.

At page 13 of the response, Applicants argue that the specification clearly describes the use of magnetisable particles to treat a disorder and in the regeneration of a tissue, such as cartilage, by associating a magnetisable particle with an ion channel of a cell. Specifically, Example 4 describes studies demonstrating the ability of a magnetic field to alter calcium channel activity following attachment of antibody-labeled magnetic particles to cells transfected.

In addition, Applicants argue that the inventors have succeeded in both up-regulating the gene osteopontin in stem cells *in vitro* and in growing cartilage in an animal model. The declaration of Professor Alicia El Haj discloses an anti-TREK antibody bound to magnetic nanoparticles binding to TREK channel in mesenchymal cells and production of cartilage in mice in response to application of an external magnetic field.

Applicant's claim amendments have been fully considered but are not found persuasive.
Although Example 4 provides evidence that the magnitizable particles bound to an antibody
affect calcium channel activities in vitro, Applicants have not provided any example and
guidance for the in vivo treatment of a disorder by administering magnitizable particles bound to
an antibody affecting calcium channel activities. The specification does not provide any
guidance on how in vitro experimentation correlate with the in vivo treatment of patients with
disorders.

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In addition, the other treatment methods claimed in the instant application are not enabled as well. Although Applicants have provided evidence for a method of A) up-regulation of osteopontin in response to a magnetic field in the presence of anti-TREK antibody bound to magnetic nanoparticles binding to TREK channel in mesenchymal cells, and (B) the production of cartilage in mice by implanted human mesenchymal stem cells in the presence of magnetic nanoparticles bound to cells via an anti-TREK antibody in response to time varying magnetic fields, Applicants have not provided any guidance, any example, level of predictability for the different claimed treatment methods including A) a method of treating a patient suffering from a disorder involving an ion channel, (B) a method of regenerating tissue, (C) a method of regenerating cartilage, (D) a method of treating a patient by destroying cells, inhibiting cell growth, or inducing osmotic shock to a cell, (E) a method of destroying tumor cells, (F) a method of killing cells by opening and closing ion channels, (G) a method of using ion channels to repair tissue and bone, and (H) a method comprising the generation of artificial tissue.

Without any sufficient disclosure of the disorders and in vivo use of the magnetizable particles, the Examiner has determined that the numerous claimed treatment methods require undue experimentation because Applicants have not provided any guidance, any working example, or any level of predictability for any of the methods treating a subject. For instance, the specification does not provide any guidance regarding the destruction or inhibition of cells, or any of the specific steps associated with the regeneration of artificial tissue with administration of magnetizable particles. In another instance, the specification does not provided any guidance as how magnetizable particles bound to ion channels can be used to regenerate tissue like bone, cartilage, or ligament.

In addition, Applicants have not overcome the unpredictability in the art. As disclosed at page 10 of the last Office action (mailed 07/12/2007), numerous references point to the

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unpredictability of treating disorder by targeting ion channels with magnetic particles. For instance, the reference by Komarova et al. (2001) teaches that ion channels on osteoclasts can be a potential target for antiresorptive drugs. It is conceivable that agents will be identified that target specifically to bone or interact selectively with osteoclast ion channels to inhibit resorption in metabolic and inflammatory bone diseases (page 651, right column bottom of last paragraph). The state of the art regarding the role of ion channels in bone metabolism is still not predictable. While the art provides limited experimental evidence for the role of ion channels in wound healing and in bone repair, the specification does not provide any link, connection, or evidence that magenisable particles can be used in a method for the treatment of a tissue/bone repair, tissue generation, wound healing/tissue adhesion as recited in the claimed invention.

Moreover, the declaration under 37 CFR 1.132 filed 01/08/2008 is insufficient to overcome the rejection of claims 46, 49-50, 59-64, 68-69, and 71 newly added claims 26, 28-29, 31-32, 36-37, 39-40, 43, 45 and 154-174 based upon 35 USC 112, First paragraph (Enablement) because Applicants have not provided sufficient guidance, so that one skilled in the art can use the claimed invention. In the declaration filed 01/08/2008, Exhibit A shows an experiment resulting in the up-regulation of osteopontin in response to a magnetic field in the presence of anti-TREK antibody bound to magnetic nanoparticles binding to TREK channel in mesenchymal cells. In addition, Exhibit B shows the production of cartilage in mice by implanted human mesenchymal stem cells in the presence of magnetic nanoparticles bound to cells via an anti-TREK antibody in response time varying magnetic fields. However, Applicants have not provided evidence that the claimed method of treatment can be successfully performed. Although Exhibit B discloses the synthesis of cartilage by mesenchymal cells in mice, there is no evidence that the cartilage can be used to repair cartilage defects. From the art, the model is not accepted in the art. Moreover, Applicants acknowledge in the declaration

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that Exhibit B "demonstrates the potential of the technique for treating cartilage defects caused either by trauma or disease". Thus the claimed treatment method is still unpredictable and required undue experimentation.

Furthermore, it would require undue experimentation for one of skill in the art to be able to make/use the claimed treatment methods because Applicants have not provided any structural and functional identifying characteristics for the disorder, ion channel, magnetisable particles, therapeutically active agent, magnetic core with a biocompatible coating, antibodies, protein binding motifs, transmembrane extracellular matrix molecule, and immunoglobulin recited in the claimed treatment methods.

The specification does not provide any correlation between the structural features and the functional activities of the disorder, an ion channel, magnetisable particles, a therapeutically active agent, a magnetic core with a biocompatible coating, antibodies, protein binding motifs, a transmembrane extracellular matrix molecule, and an immunoglobulin recited in the claimed methods, so that one skilled in the art would not be able to predict that all possible magenetizable particles, ion channels, and any antibodies can treat any disorders. For instance, the specification teaches that the method of treatment which is applicable to any disorder in which one or more ion channels play a role (page 8, line 25) and that channels are generally characterized by their ionic selectivity for example, sodium channel, potassium channel, calcium channel, chloride channel, non-selective cation channel (page 1 lines 16-21) and that more than 50 types of ion channels have been identified (page 1 lines 31-32). Thus it would require undue experimentation to practice the invention commensurate in scope with the claims because the claims are broadly drawn to any magenetizable particles, any ion channels, and any antibodies utilized in the claimed method.

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Furthermore, it would require undue experimentation to practice the invention commensurate in scope with the claims because, the claims are broadly drawn to a method of treating a patient suffering from a disorder involving an ion channel comprising administering a magnetizable particle. The specification's general discussion of using magnetizable particles to treat a disorder and in the regeneration of a tissue by associating a magnetizable particle constitutes an invitation to experiment by trial and error. Such experimentation is considered to be undue.

Finally, due to the large quantity of experimentation necessary to determine the quantity of magnetizable particles to be administered, the most effective administration route, and the duration of the treatment, the lack of direction/guidance presented in the specification regarding the same, the absence of working examples directed to the same, the complex nature of the invention, and the unpredictability of the effects of the magnetizable particles in vivo, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Claim Rejections - 35 USC § 112, Second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 46, 49-50, 59-64, 68-69, 71 and the previously non-elected claims claims 26, 28-29, 31-32, 36-37, 39-40, 43, 45 and the newly added claims 154-174 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 46, 49-50, 59-64, 68-69, and 71 remain rejected and the previously non-elected claims 26, 28-29, 31-32, 36-37, 39-40, 43, 45 and the newly added claims 154-174 are also rejected, under 35 USC 112,

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second paragraph, for the reasons already of record on pages 12-13 of the Office Action mailed 07/12/2007.

At page 14 of the response, Applicants argue that following entry of the amendments, one of skill in the art would clearly be able to determine the metes and bounds of all the pending claims, and that the rejection of the claims under 35 USC §112, second paragraph, may thus be properly withdrawn.

Applicant's claim amendments have been fully considered but are not found persuasive. Although Applicants have partially overcome the rejections under 35 USC 112, Second paragraph by amending claims 46 and 59 and cancelling claim 50, claims 46, 49-50, 59-64, 68-69, and 71 and the newly added claims 26, 28-29, 31-32, 36-37, 39-40, 43, 45 and 154-174 remain rejected, under 35 USC 112, first paragraph, for the reasons already of record on pages 13 of the Office Action mailed 07/12/2007.

At page 14 of the response, Applicants argue that the term "manipulating an ion channel", it is submitted that one of skill in the art, on being provided with the instant specification would appreciate that this term refers to changing the conformational state of the ion channel, as stated, for example, in paragraph 0031 of the published application.

Applicant's claim amendments have been fully considered but are not found persuasive. While the specification teaches that all ion channels can be activated by the method described herein provided that the magnetisable particle is coupled, either directly or indirectly, to the mechanoresponsive region of the channel protein (page 6, lines 14-23), the specification does not define "manipulating" in terms of activating or changing the conformation of the ion channel. In addition, the specification (page 6, lines 14-23), does not provide any nexus between the term "manipulating" and the conformational state of the ion channels. Therefore, the term "manipulating" in claim 46 remain indefinite.

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Claims 46, 49-50, 59-64, 68-69, 71 and the newly added claims 26, 28-29, 31-32, 36-37, 39-40, 43, 45 and 154-174 remain rejected as being indefinite because claim 46, recites the limitation "manipulating". The term "manipulating" in claim 46 is a relative term which renders the claim indefinite. The term "manipulating" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. For instance, it is unclear as to what is encompassed by the term "manipulating".

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 46 remains rejected under 35 U.S.C. 102(b) as being anticipated by Yanase et al. (1998, Japanese Journal of Cancer Research, Volume 89, pages 463-469) and the newly claim 154 is now rejected under 35 U.S.C. 102(b) as being anticipated by Yanase et al.

Yanase et al. (1998,) teach that the injection of magnetite cationic liposomes into tumors made up of soft glioma tissue and subjected to irradiation by an alternating magnetic field resulting into tumor regression (page 463, abstract) meeting the limitations of claims 46 Although the reference by Yanase et al. do not explicitly teach a disorder involving an ion channel, Ullrich et al. (1998, Neuroscience, Volume 83, Issue 4, pages 1161-1173) teach that the expression of chloride channels in human gliomas is probably a glioma-specific feature (Page 1161, last line of abstract).

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The invention is drawn to a method of treating a patient suffering from a disorder involving an ion channel comprising administering to the patient magnetisable particles, wherein the magnetizables particles associate with an ion channel of a cell of the patient; and manipulation the ion channel using a magnetic field external to the patient, thereby treating the disorder, wherein the magnetic field is a constant field or is a variable field with a frequency of 0.1 Hz to 10 Hz.

At page 15 of the response, Applicants argue that Yanase et al. do not teach or suggest the use of a magnetic field that is constant or is a variable field with a frequency of 0.1-10 HZ to manipulate an ion channel of a cell in order to treat a disorder.

In addition, Applicants argue that Yanase et al. do not teach or suggest a method of regenerating tissue by associating a magnetisable particle with an ion channel of a cell and manipulating the ion channel using a magnetic field, wherein the cell is a ligamentum cell, tenocyte, chondrocyte or stromal cell, as recited in newly added independent claim 161, nor do they teach or suggest a method for regenerating cartilage by associating a magnetisable particle with a TREK ion channel of a chondrocyte by means of an antibody, and manipulating the ion channel using a magnetic field, as recited in newly added independent claim 169.

Applicant's claim amendments have been fully considered but are not found persuasive.

Contrary to Applicants' argument, Yanase et al. teach that the magnetic field was constant at 118 kHz (page 466, left column, 1st paragraph) meeting the limitation recited in claim 46.

Please note that the Examiner is maintaining his rejection because the Examiner has been unable to determine whether the recited Hz range includes the limitation of the constant field as well as the one with the variable field. In addition, the Examiner has not included in this rejection the claims 161 or 169 reciting a method for regenerating cartilage by associating a magnetisable particle with a TREK ion channel of a chondrocyte by means of an antibody, and

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manipulating the ion channel using a magnetic field because the art does not teach such methods

Additionally, in response to applicant's arguments, the recitation "...of treating a patient suffering from a disorder involving an ion channel" disclosed in claim 46 has not been given patentable weight because the recitation occurs in the preamble. A preamble is generally not accorded any patentable weight where it merely recites the purpose of a process or the intended use of a structure, and where the body of the claim does not depend on the preamble for completeness but, instead, the process steps or structural limitations are able to stand alone.

See In re Hirao, 535 F.2d 67, 190 USPQ 15 (CCPA 1976) and Kropa v. Robie, 187 F.2d 150, 152, 88 USPQ 478, 481 (CCPA 1951).

Yanase et al. (1998.) teach that the injection of magnetite cationic liposomes into tumors made up of soft glioma tissue and subjected to irradiation by an external magnetic field resulting into tumor regression (page 463, abstract) meeting the limitations of claim 46. Although the reference by Yanase et al. do not explicitly teach a disorder involving an ion channel, Ullrich et al. (1998, Neuroscience, Volume 83, Issue 4, pages 1161-1173) teach that the expression of chloride channels in human gliomas is probably a glioma-specific feature (Page 1161, last line of abstract).

Conclusion

No claim is allowed

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Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to IAN DANG whose telephone number is (571)272-5014. The examiner can normally be reached on Monday-Friday from 9am to 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Manjunath Rao can be reached on (571) 272-0939. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

lan Dang Patent Examiner Art Unit 1647 March 24, 2008

> /Robert Landsman/ Primary Examiner, Art Unit 1647